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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,325	11/18/2003	Anita Liberman	1662/61702	8274

26646 7590 10/09/2008

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EXAMINER	
MORRIS, PATRICIA L	
ART UNIT	**PAPER NUMBER**
1625	
MAIL DATE	**DELIVERY MODE**
10/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/717,325	LIBERMAN ET AL.	
	Examiner	Art Unit	
	Patricia L. Morris	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-40* is/are pending in the application.

4a) Of the above claim(s) *8-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 29-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/14/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-6 and 29-40 are under consideration in this application.

Claims 8-28 remain held withdrawn from consideration as being drawn to nonelected subject matter 37 CFR 1.142(b).

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 14, 2008 has been entered.

Election/Restrictions

The restriction requirement is deemed sound and proper and is hereby maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6 and 29-40 are rejected under 35 U.S.C. 102(a), (b) and/or (e) as being anticpated by Vrecer et al., Kotar et al., Choi et al., Nohara et al., Kato et al. and Avrutov et al. I, II. for the reasons set forth in the previous Office action.

Again, Vrecer et al., Kotar et al., Choi et al., Nohara et al., Singer et al., Kato et al. and Avrutov I, II specifically disclose the instant compound and compositions. Note, example 1 of Choi et al. or claim 7 of Kato et al.. Hence, the instant compound is deemed anticipated therefrom.

The instant pharmaceutical compositions containing the claimed compound would be the same as the prior art pharmaceutical compositions containing lansoprazole, since the claimed lansoprazole would no longer exist in solution, or after granulation, compaction or tableting processes, as it is well known in the art that such processes would lead to alteration of the solid form. Note, for example, Chemical & Engineering News, pages 33-34.

The declaration of Singer filed July 14, 2008, while interesting, is of little if any probative value because it only includes only the prior art compound of Kato and fails to include any of the other prior art compounds. The showing is not **side-by-side** with the claimed compounds containing the stable lansoprazole. Further, the declaration fails to show that pharmaceutical compositions containing the stable compound are any different from the prior art compositions upon administration to a physiological environment. It is well known in the art that crystalline forms will lose their unique crystalline lattice especially upon administration in a physiological environment.

Claim Rejections - 35 USC э 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6 and 29-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Vcer et al., Kotar et al., Choi et al., Nohara et al. Singer et al., Kato et al ., and Avrutov et al. I, II in view of Hableblian et al, Chemical & Engineering News, US Pharmacopia, , Muzaffar et al., Jain et al. Taday et al. and Concise Encyclopedia Chemistry for the reasons set forth in the previous Office action.

Again, the references teach the stable crystal forms of the instant known compound and as well as the pharmaceutical compositions. Note claim 7 of Kato et al., example 1 of Choi et al. or example 3 of Avrutov et al. II . Habeblian et al., Muzaffar et al., Jain et al. and Taday et al. teach that the compounds exist in different crystalline

forms. Chemical & Engineering News, Muzaffar et al., US Pharmacopia and Concise Encyclopedia teach that at any particular temperature and pressure, only one crystalline form is thermodynamically stable. Hence the claimed crystalline form as well as its relative selectivity of properties *vis-a-vis* the known compound are suggested by the references. It would appear obvious to one skilled in the art in view of the references that the instant compound would exist in different stable crystalline forms. No unexpected or unobvious properties are noted.

Applicants assert that they are claiming a chemically stable compound. As discussed supra, applicants have failed to shown in the declaration that the claimed compounds vis-a-vis the **prior art compounds cited in the references of record** are more stable than the prior art compounds. The declaration only includes the compound of Kato et and fails to include the claimed compound. Further, applicants claims are drawn to stability for at least six months and yet the declaration does not show this. The declaration is silent as to how the compositions containing the claimed lansoprazole have any different unexpected or unobvious properties as the pharmaceutical compositions containing the prior art lansoprazole.

Claim Rejections - 35 USC э 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-38 and 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement and enablement. The claim(s)

contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, or was not described in the specification in such a way to enable one skilled in the art to which it pertains, or which it is mostly nearly connected, to make and/or use the invention.

Again, there is a lack of description as to whether the compositions are able to maintain the compound in the stable form claimed. Again, the specification lacks description or enablement as to the whether the stable forms are thermodynamically stable as to provide utility at room temperature for these stable forms in the pharmaceutical compositions. Contra to applicants' arguments in the instant response, applicants have **failed to provide any objective evidence that the instant stable form is indeed maintained in the pharmaceutical compositions.** Applicants merely assert that the instant compounds are not polymorphs. However, the instant compounds behave similarly to polymorphs. The specification lacks description that the pharmaceutical compositions contain the "**stable form**" without transformation in the pharmaceutical compositions. The pharmaceutical formulation field is well aware that forms when formulation into compositions may undergo transformation thus, the particular form may not be the same form after processing, compressing, etc. Note the prior art references of record.

The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. Applicants are referred to In re Fouche, 169 USPQ 429 CCPA 1971, MPEP 716.02(b).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention

The nature of the invention is the preparation of a chemically stable compound.

State of the Prior Art

The pharmaceutical formulation field is well aware that compounds when formulated into compositions may under transformation, thus a particular form may not be the same after processing, compressing, etc., (See Chemical Engineering News, pages 43-35. Therefore, in absence of any description or factual evidence, how a crystalline form can be maintained in a composition to minimize transformation, no assumption can be made that the alleged stable form will be maintained upon compression, tableting, etc.

The amount of direction or guidance and the presence or absence of working examples

The specification fails to disclose that asserted stable compound in the pharmaceutical compositions is maintained upon administration in a physiological environment.

The breadth of the claims

The breadth of the claim are drawn to the specific stable form and in addition to the pharmaceutical compositions.

The quantity of experimentation needed

The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the pharmaceuticals compositions being claimed and verifying that the stable form stays in the same form.

Claims 29-38 and 40 are drawn to pharmaceutical composition comprising a stable compound keeping its crystalline property. The field of pharmaceutical composition of crystalline product is highly unpredictable and empirical. Yet, applicants are claiming compositions containing the stable form and the specification is silent as to the preparation of compositions containing a minimum amount of the form without any specific description of the specific excipients and processing parameters, that such form can be made into a composition. One of ordinary skill in the art would read that claims 33-38 each contain the form recited therein. Applicants argue that the pharmaceutical compositions do not contain **polymorphic forms**. **The examiner is well aware that the stable form of lansoprazole is not a polymorph. However, the alleged stable form is in crystalline form and it is well known in the art that crystalline forms will lose their unique crystalline lattice upon compaction, tableting, etc.** However, applicants' own specification specifically state that the excipent may be a diluent or solvent. Jain et al. on page 316 clearly states that *"when a cystalline solid is dissolved in solvent, the crystalline structure is lost so that different polymorphs of the same substance will show*

the same absorption spectra as solution". Further, in the aqueous phase, *all physical forms are amorphous* (see Ulicky).

It is well known in the art, at a given pressure and temperature only one thermodynamically stable crystalline form will exist for a given compound (see Concise Encyclopedia supra and US Pharmacopia). Hence, it is expected in the art that when a crystalline form for a drug is prepared into a solid formulation, *unless specific and* particular conditions can be described, the "form" is expected to change to the most thermodynamically stable one.

The state of the pharmaceutical composition containing polymorphic form art provided per ponderous of evidence that *unless specific and particular* conditions can be obtained, the formulation process would cause polymorphic forms to change.

See :

> --Muzaffar et al. p.60 "At any one temperature and pressure only one crystal form of a drug is stable and any other polymorph existing under these conditions will convert to the stable form .... " And p.63-65 (a)-(h) pharmaceutical preparing processes affect polymorphism;
>
> --Jain et al. p.322-326, manufacturing processes that affect polymorphs ;
>
> ----Doelker et al. abstract (english translation now provided)
> "...a given drug, although chem. well defined, may exhibits quite different behavior. Process conditions (grinding, tableting, granulations, drying) may also affect secondary properties of the drug, such as compactibility, wetttability, solvent, dissolution rate, bioavailability and even pharmacological, activity."
>
> --Otsuka et al. p.852 ...in formulation studies and the method preparing CBZ has been shown to affect the drug's pharmaceutical properties through the polymorphic phase transformation of the bulk CBZ powder during the manufacturing process"
>
> Taday et al. p. 831 states "Once in the desired crystalline form, the polymorphis state *may be changed* by incorrect storgage or even during tablet preparation and

> p. 836, figure 8, wherein compound of four form in pharmaceutical composition resulted in similar spectra, *i.e.,* form.

The pharmaceutical composition field has well recognized that stability of an active principle i.e. specific form of a compound, has no predictability on its outcome in composition processing. It is known in the art that:

> --Singhal et al. "..It should be pointed out that a major portion of any formulation effort is the choice of exipients and processes which minimize the chemical instability of the drug…." P.338, left col.

On pages 9- 10 of the specification, it was explicitly disclosed that for the pharmaceutical compositions of the crystalline forms, the carriers are selected from generally known excipents ……." and on page 11 to form into suspension, liquid syrups, etc. Note that all liquids are non-crystalline, thus, are known to abolish the forms unique crystalline lattice.

The specification has provided no description or enablement as to how the newly acquired "form" can be prepared into a composition which can maintain the particular crystalline structure without the conventional recognized conversion to other forms i.e. amorphous form in liquid, emulsion etc. Per ponderous of evidence in the prior art indicated that for a given polymorph, *absent of any description or enablement* from the specification, does not *automatically* keeps its form in the pharmaceutical composition. The specification is silent as to what specific excipents and preparation conditions are employed to form the composition containing the specific stable form.

In view of the per ponderous of evidence as delineated supra, it is well recognized in the art that for a given crystalline form of a drug, *in absence of explicit* enabling description, in view of the high degree of unpredictability, even if one is in possession of

a particular crystalline form, no predictability can be found that such forms will prevail in pharmaceutical compositions.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 and 29-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Again, the expressions "comprising" and "comprises" in claims 1-6 and 39 is open-ended and allows for the inclusion of other parameters not contemplated by applicants. Contra to applicants' arguments, the claims are drawn to compounds only. Applicants merely assert that the examiner has interpreted the term compound very narrowly. This is certainly not persuasive because the instant claims are drawn to an alleged stable compound only.

Applicants are claiming a compound of the formula. Pure chemistry, a compound. Not a resin of general property ranges, but a pure compound. That compound used for any purpose is taken from the public in a 20-year monopoly to applicants. Then, the public is entitled to know what compound they cannot use. Yet, the claim is not specific to that compound. The public cannot tell what they may not use. How is the claim of the instant breadth defensible in an infringement action?

As applied to pure compounds, In re Cavallito and Gray, 134 USPQ 370, and In re Sus and Schaefer, 134 USPQ 301, are considered to set the proper applicable standard of required definiteness and support.

Again, claims 1-6 and 29-40 contains the generic name lansoprazole. Where a generic name is used in a claim as limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the generic name cannot be used properly to identify any particular material or product. A generic name is used to identify a source of goods, and not the goods themselves. In the present case, the generic name is used to identify/describe a compound having a specific chemical structure and, according, the identification/description is indefinite. Contra to applicants' arguments in the instant response, the name does **not** define the chemical structure of the compound.

The claims measure the invention. United Carbon Co. V. Binney & Smith Co., 55 USPQ 381 at 384, col. 1, end of 1st paragraph, Supreme Court of the United States (1942).

The U.S. Court of Claims held to this standard in Lockheed Aircraft Corp. v. United States, 193 USPQ 449, The claims measure invention and resolution of invention must be based on what is claimed.

The C.C.P.A. in 1978 held that an invention is the subject matter defined by the claims submitted by the applicant. We have consistently held that no applicant should have limitations of the specification read into a claim where no express statement of the limitation is included in the claim. In re Priest, 199 USPQ 11, at 15.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1- and 29-40 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 33-38 and 41-45 of copending Application No. 10/773,535 in view of Haleblian et al., Chemical & Engineering News, US Pharmacopia, Muzaffar et al., Jain et al., Taday et al. and Concise Encyclopedia Chemistry for the reasons set forth in the previous Office action..

This is a provisional obviousness-type double patenting rejection.

Again, Ser. No 10/773,535 disclose the instant stable compound and compositions. Hence, patentable distinction is not seen.

Again, a terminal disclaimer has not been received too date.

Claim Objections

Claims 6, 34, 39 and 40 are objected to because of the following informalities: The term pyridinyl is misspelled. Appropriate correction is required.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia L. Morris whose telephone number is (571) 272-0688. The examiner can normally be reached on Mondays through Fridays.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Patricia L. Morris/
Primary Examiner, Art Unit 1625

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October 7, 2008